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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,117	07/22/2002	Gerard Giordano	0508-1004	8083

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,117	GIORDANO ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-12 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 4/25/2005 is acknowledged. The traversal is on the ground(s) that the definition of "special technical feature" is art based. This is not found persuasive because as evidenced below, the elected claims are not patentable over the cited references, and as such do not provide a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

2. An action on the merits of claims 1-6, 10-12, and newly added claims 16-18 are set forth below.

Claim Rejections - 35 USC § 112

Indefinite

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-6, 10-12, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 lacks a positive process step relating back to the preamble. The preamble states a method of detecting the presence of "all" bacteria involved in the process of degradation of the flesh of aquatic animals, however the positive step only sets forth detection of a nucleic acid of the TMAO reductase system in bacteria. Accordingly, it is unclear what method the claims are drawn to. Claim 1 is further indefinite in the recitation of "all bacteria" because it is unclear if the claims are meant to encompass all bacteria found in any single animal, or all bacteria in

general. The lack of clear active process steps makes the metes and bounds of the detection step confusing. Accordingly, the metes and bounds of the claim are unclear.

Claim 1 recites "TMAO reductase system", however the metes and bounds of such recitation is unclear. The specification does not define the metes and bounds of TMAO reductase "system" therefore it cannot be determined which enzymes are encompassed by the claims. For example, does it only refer to a TMAO reductase, or does it encompass any enzyme or protein involved with the metabolism (synthesis or break down) of trimethylamine N-oxide.

Claim 1 recites the term "suppression" in the context of a nucleic acid sequence. This term is indefinite because it is unclear how a nucleic acid is "suppressed". The structural implications on the nucleic acid cannot be determined by the recitation.

The use of the term "capable of hybridizing" in claim 1 is indefinite because the word "capable" describes latent characteristics. Thus it is unclear if the sequences do in fact hybridize to a nucleic acid in the method of claim 1 and is meant as a positive active step, or if it simply describes a characteristic of a sequence. As claim 1 only recites "detecting" as a positive active step, it is unclear if further language in claim 1 is meant to be drawn to positive active steps in the method.

Claims 2-4 recite "the method to claim 1". It appears to be missing the term "according".

Claim 2 is indefinite in the recitation of "further designated". It is unclear if the term is meant to limit claim 2 to TorA or DorA, or TorC or DorC, or if such are set forth as examples of possible proteins, but the claims can encompass other sequences. It is unclear if the recitation of "further designated" was meant as Markush type language. If this is the case, the terms should be amended to recite instead to "selected from the group consisting of".

Claim 3 is indefinite because it is unclear if the term "such as" is meant to limit the bacteria in the claims to those listed. Additionally, the claim refers to figures which is unclear because it cannot be determined whether the claim means to limit the proteins to the specific sequences listed in the figure or not. The claim should be amended to include a proper SEQ ID NO: and to make clear whether, for example, "TorA protein of Shewanella massilia" refers to a specific SEQ ID NO.

Claims 4 and 16-18 are indefinite because it cannot be determined whether the claim is limited to all the sequences in a "group of primers". The designation of "mixture of X nucleotide sequences" is confusing because it is unclear if the recitation means to limit the sequences used to all sequences in the mixture, or to one or more sequences in the mixture. As such, the use of the degenerate SEQ ID NOS is confusing because the use of such appears to imply a single sequence. Accordingly, the metes and bounds of the claim are unclear because it is not clear how many primers are used in the method. Additionally the use of "in particular from" at the bottom of page 6 of claims submitted 4/25/2005 is confusing because it is not clear if the claim is limited to the embodiments listed on page 7 or not. Use of language "such as" 'in particular from", "especially", etc, while not per se indefinite, is confusing and unclear in the instant claims (see claim 5 as well) because it cannot be determined whether the added recitations following such language is meant as a claim limitation or not.

Claim 6 is indefinite because it is unclear what method steps are encompassed by "in the framework of a method...". The claim sets forth no positive active steps. It is not clear how it further limits the claim from which it depends.

Claim 10 is generally narrative and lacks positive active steps. It appears to be a translation. For example, the recitation of "said method being effected", the recitation of "corresponding in particular to a subcutaneaous fragment", "being characterized in that it comprises", "in particular by electrophoresis", etc are indefinite because it is not clear if the recitation of such is meant to limit the claim to a particular embodiment or not.

Claims 11 and 12 are indefinite as it is unclear what steps, reagents, and parameters the method is required to be limited to. Use of the phrases "in particular using", "in order to", "based on fixation of", "aforementioned", "preferably", "in claims 1-9" (claim 12), "for example" are unclear because it is not clear what actual steps, reagents, and parameters the claims are limited to.

With regard to claims 1-6, 10-12, and 16-18, as set forth above, the claims are generally narrative and appear to be a translation of a foreign patent document, and fail to conform to USPTO standards. The lack of positive active steps (in some cases), as well as the use of phrases "such as", "in particular", etc in almost all cases renders the metes and bounds of the methods unclear. The scope of the claims are unascertainable due to the use of such language as well as the omission of clear positive active steps.

Written Description

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 10-12, and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims appear to be drawn to methods of detecting all bacteria involved in the process of degradation of the flesh of aquatic animals using nucleic acid sequences to the TMAO reductase system in any bacteria. It is unclear, however, if the claims are meant to encompass all bacteria found in any single animal, or all bacteria in general. Additionally, it is unclear what specific sequences the claims are drawn to.

The specification teaches the sequences of the TorA, TorC, and TorD sequences of a new species of bacteria: *Shewanella massilia*, as well as several homologous sequences from other species of bacteria including *E. coli*. The specification also teaches partial TorA sequences from certain bacteria such as *Photobacterium phosphoreum*, and *Salmonella typhimurium*. The specification teaches the sequences of degenerate primers and detection of specific bacteria (page 26), however the specification is silent with regard to which specific primer pairs were used in detection. The specification only lists the general degenerate sequence, but does not teach which specific primer pair was used to detect different bacteria. Additionally, while the specification teaches the sequence of specific TMAO reductases, the specification does not teach the use of sequences that are generally involved in the TMAO reductase system. It is not clear from the recitation in the specification as to which sequences other than the TorA, TorC, and TorD

sequences would be encompassed by the TMAO reductase "system" or whether the use of the term "system" is meant to designate just TorA, TorC, and TorD from bacteria.

The claims as written encompass methods of detecting a large genus of sequences using a large genus of primers and probes which are not represented by the specific disclosure in the specification. For example, it is clear from Table 1 that sequences to degenerate primers are listed in the claims which do not detect "all" bacteria involved in degradation of the flesh of aquatic animals. As such, the specification fails to teach any methods that detect "all bacteria" as specified in the claims, using *any* of the primers listed in the claims: for example BN1+/BN2-. Additionally, the specification does not teach which specific primer sequences were used to detect the bacteria in table 1. The specification does not teach which specific sequences were used to achieve detection in the specification. While the claims recite "mixtures" with regard to the degenerate sequences, it is unclear if all the primers of a mixture were used, or only specific ones. If the latter is the case, the specification is silent with regard to any specific combination. Further, the claims are also broadly drawn to using any enzyme involved in the TMAO system, from any bacteria involved in degradation of the flesh of aquatic animals, and thus encompass the use of sequences from bacteria yet to be discovered, as well as sequences from known bacteria yet to be determined. As exemplified by the teachings in the specification, only partial sequences have been taught for certain bacteria, while other sequences have not been taught. For example, TorD for Shewanella massilia is not taught, nor are any sequences for Vibrio genus taught. Additionally, Dos Santos et al (J. Mol. Biol. vol. 284, pages 421-433) teach that the Shewanella genus can be divided into 4 groups (page 429, col. 1, 2nd full para), however the specification does not teach or describe sequences of the TMAO reductase "system" for this

broad group. It is clear from the teachings in the specification and the art that new species of bacteria are being discovered, and that the claims broadly encompass methods of using sequences from species which are as yet unknown. The description of such sequences is needed in constructing adequate probes and primers that would be capable of detecting all bacteria involved in the degradation of the flesh of aquatic animals.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the

written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

7. Claims 1-6, 10-12, and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims appear to be drawn to methods of detecting all bacteria involved in the process of degradation of the flesh of aquatic animals using nucleic acid sequences to the TMAO reductase system in any bacteria. It is unclear, however, if the claims are meant to encompass all bacteria found in any single animal, or all bacteria in general. Additionally, it is unclear what specific sequences the claims are drawn to.

The specification teaches the sequences of the TorA, TorC, and TorD sequences of a new species of bacteria: *Shewanella massilia*, as well as several homologous sequences from other species of bacteria including *E. coli*. The specification also teaches partial TorA sequences from certain bacteria such as *Photobacterium phosphoreum*, and *Salmonella typhimurium*. The specification teaches the sequences of degenerate primers and detection of specific bacteria (page 26), however the specification is silent with regard to which specific primer pairs were used in detection. The specification only lists the general degenerate sequence, but does not teach which specific primer pair was used to detect different bacteria. Additionally, while the specification

teaches the sequence of specific TMAO reductases, the specification does not teach the use of sequences that are generally involved in the TMAO reductase system. It is not clear from the recitation in the specification as to which sequences other than the TorA, TorC, and TorD sequences would be encompassed by the TMAO reductase "system" or whether the use of the term "system" is meant to designate just TorA, TorC, and TorD from bacteria.

The claims as written encompass methods of detecting a large number of sequences using a large number of possible primers and probes for which the specification does not provide adequate guidance. For example, it is clear from Table 1 that sequences to degenerate primers are listed in the claims which do not detect "all" bacteria involved in degradation of the flesh of aquatic animals. As such, the specification fails to teach any methods that detect "all bacteria" as specified in the claims, using *any* of the primers listed in the claims: for example BN1+/BN2-. Additionally, the specification does not teach which specific primer sequences were used to detect the bacteria in table 1. The specification does not teach which specific sequences were used to achieve detection in the specification. While the claims recite "mixtures" with regard to the degenerate sequences, it is unclear if all the primers of a mixture were used, or only specific ones. If the latter is the case, the specification is silent with regard to any specific combination. Further, the claims are also broadly drawn to using any enzyme involved in the TMAO system, from any bacteria involved in degradation of the flesh of aquatic animals, and thus encompass the use of sequences from bacteria yet to be discovered, as well as sequences from known bacteria yet to be determined. As exemplified by the teachings in the specification, only partial sequences have been taught for certain bacteria, while other sequences have not been taught. For example, TorD for Shewanella massilia is not taught, nor are any sequences for Vibrio genus

taught. Additionally, Dos Santos et al (J. Mol. Biol. vol. 284, pages 421-433) teach that the Shewanella genus can be divided into 4 groups (page 429, col. 1, 2nd full para), however the specification does not teach or describe sequences of the TMAO reductase "system" for this broad group. It is clear from the teachings in the specification and the art that new species of bacteria are being discovered, and that the claims broadly encompass methods of using sequences from species which are as yet unknown. A teaching of such sequences is needed in constructing adequate probes and primers that would be capable of detecting all bacteria involved in the degradation of the flesh of aquatic animals.

Therefore it would take undue experimentation for one of skill in the art to practice the invention as broadly as it is claimed. The skilled artisan would be required to perform a large amount of unpredictable trial and error analysis to determine which specific sequences would be capable of carrying out the methods as broadly as they are claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-6, 10-12, and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Dos Santos (Dos Santos et al; J. Mol. Biol. vol. 284, pages 421-433).

Dos Santos teaches a method of analysis of the TorA gene from Shewanella massilia from marine fish (see 422, col.2) which included DNA extraction, PCR amplification, sequence

analysis and electrophoresis (see page 424, col 2; figure 2; pages 430-431). The recitation of the claims makes the metes and bounds of the claims unclear with regard to any specific method steps, reagents, or parameters (see 112/2nd rejections set forth above), including the sequences of any particular primers. Accordingly, the claims have been broadly interpreted to encompass the methods of Dos Santos.

10. Note: Amendment of the claims to include positive active steps as well as clearly setting forth which specific sequences are encompassed by the claimed methods as well as specific primer pairs, could overcome the rejection made under 35 USC 102(b). However, given the recitation in the instantly pending claims the examiner has been unable to ascertain the metes and bounds of the claims or what applicants intended methods encompass.

Conclusion

11. No claims are currently in condition for allowance and are rejected for the reasons set forth above.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton

Jehanne Sitton
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7/11/05